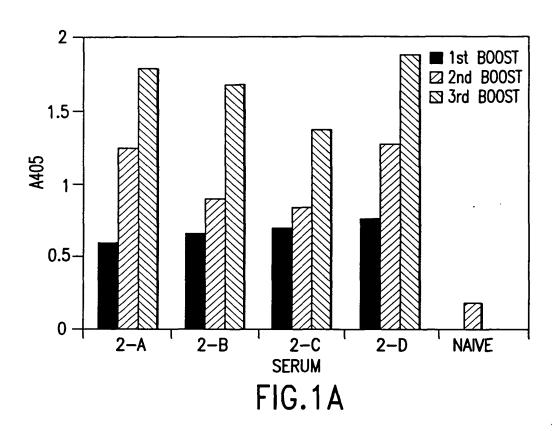
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Application No. For

Confirmation No. Not yet assigned Express Mail Label No. EV 133109365 US EV 133109365 US No. EV 133109365 US Standard Filed Concurrently herewith Sheet 1 of 11 USE OF TRANSGENIC MICE FOR THE EFFICIENT ISOLATION OF NOVEL HUMAN MONOCLONAL ANTIBODIES WITH NEUTRALIZING ACTIVITY AGAINST PRIMARY HIV-1 STRAINS AND NOVEL HIV-1 NEUTRALIZING ANTIBODIES ABX-PHRI CON Reg. No. 43,753

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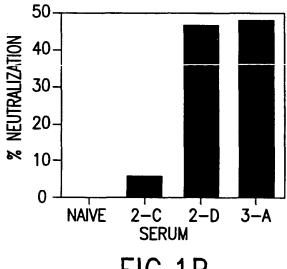
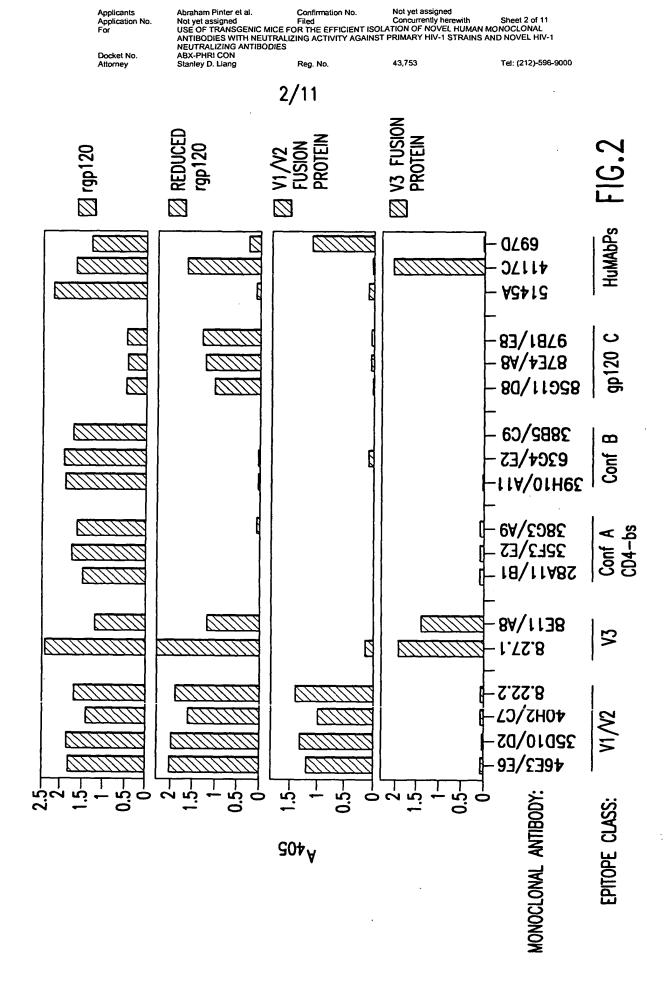


FIG.1B



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USE OF TRANSGENIC MICE FOR THE EFFICIENT ISOLATION OF NOVEL HUMAN MONOCLONAL

ANTIBODIES WITH NEUTRALIZING ACTIVITY AGAINST PRIMARY HIV-1 STRAINS AND NOVEL HIV-1

NEUTRALIZING ANTIBODIES

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Reg. No.

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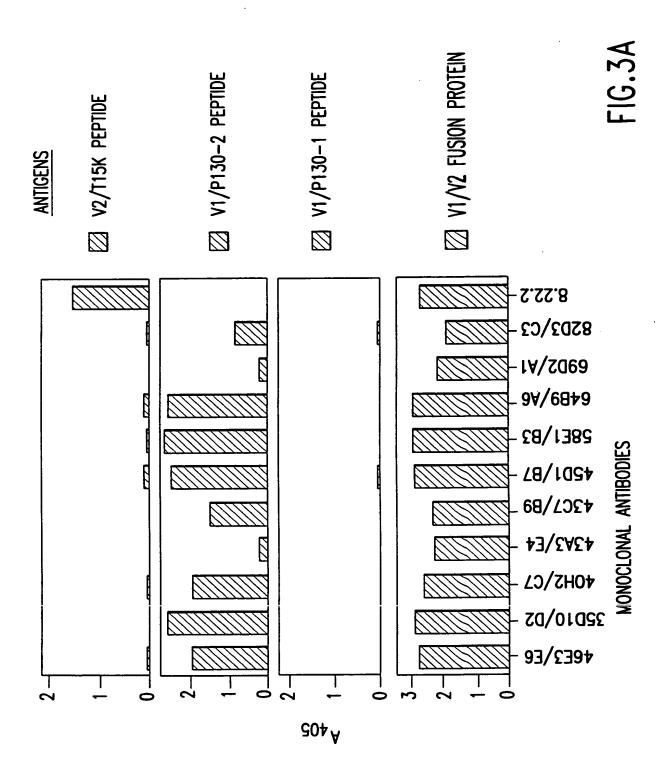
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ANTIBODIES WITH NEUTRALIZING ACTIVITY AGAINST PRIMARY HIV-1 STRAINS AND NOVEL HIV-1
NEUTRALIZING ANTIBODIES
ABX-PHRI CON
Stanley D. Liang
Reg. No.
43,753
Tel: (212)-596-5 Docket No. Tel: (212)-596-9000 Attorney :: **9** ;; SEQ 1D NO: SEQ 1D NO: SEQ 1D SEQ 10 LKPCVKLTPLCVTLHCTNL KNATNTKSSNWKEMDRGEIKNCSF KVTTSIRNKWQKEYALFYKLDVVPIDNDNTSY KLINCNTSVITQACPKVS RIGHT STEM TTSIRDKVQKEYALFYK 72

CENTRAL

5

NTKSSNWKEND GEIK

P130-1 P130-2 T15K

STNL KNATNTKSSNW

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USE OF TRANSGENIC MICE FOR THE EFFICIENT ISOLATION OF NOVEL HUMAN MONOCLONAL

ANTIBODIES WITH NEUTRALIZING ACTIVITY AGAINST PRIMARY HIV-1 STRAINS AND NOVEL HIV-1

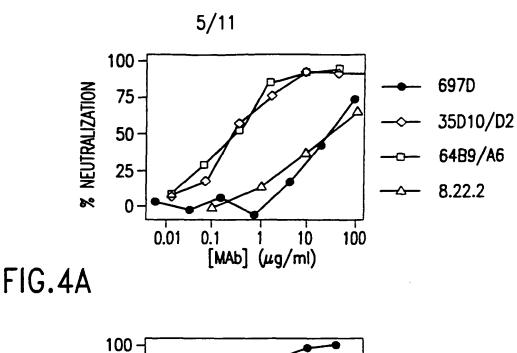
NEUTRALIZING ANTIBODIES ABX-PHRI CON Stanley D. Liang

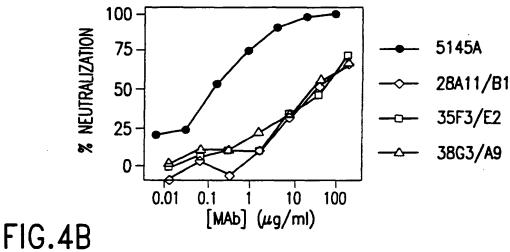
Docket No. Attorney

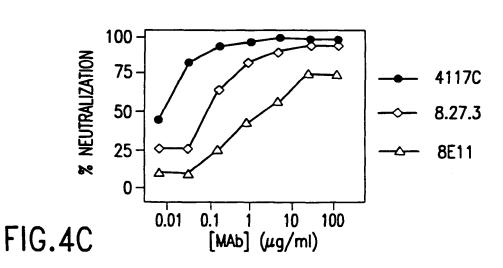
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USE OF TRANSGENIC MICE FOR THE EFFICIENT ISOLATION OF NOVEL HUMAN MONOCLONAL

ANTIBODIES WITH NEUTRALIZING ACTIVITY AGAINST PRIMARY HIV-1 STRAINS AND NOVEL HIV-1

NEUTRALIZING ANTIBODIES

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COMPET	ING Mab	% INHIB	ITION OF BIND	ING BY	BIOTINYLATED
EPITOPE	NAME	43A3/E4	35D10/D2	697D	sCD4
	35D10/D2	89	89	7	26
	40H2/C7	82	83	5	13
	43A3/E4	78	82	9	10
	43C7/B9	82	83	8	13
	45D1/B7	85	85	11	17
V1 LINEAR	46E3/E6	86	86	9	-29
	58E1/B3	88	88	4	21
	64B9/A6	89	89	12	24
	69D2/A1	58	65	12	37
	82D3/C3	52	56	11	-35
V2 LINEAR	8.22.2	1	1	84	-1
V2 CONF.	697D	3	-5	83	6
	SC258	9	21	45	0
V 3	8.27.3	9	24	11	9
CD4bs	5145A	0	11	-55	93

FIG. 5

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USE OF TRANSGENIC MICE FOR THE EFFICIENT ISOLATION OF NOVEL HUMAN MONOCLONAL
ANTIBODIES WITH NEUTRALIZING ACTIVITY AGAINST PRIMARY HIV-1 STRAINS AND NOVEL HIV-1
NEUTRALIZING ANTIBODIES

ABX-PHRI CON
Stanlev D Liner Applicants Application No. For Docket No Reg. No. Tel: (212)-596-9000 Attorney Stanley D. Liang 43,753 7/11 21-40 0.00 0.05 0.06 0.05 0.05 0.12 0.05 0.01 0.03 0.03 5122 _____ <u>5</u> 0.03 1.72 0.05 0.06 0.12 0.07 0.07 SEQ SEQ SEQ YTTKNI IGTIRQAHCNI SRA **--**20 0.30 2.72 0.01 0.04 3.26 2.60 1.94 2.53 2.10 3.51 CTRPSNNTRKS1H1GPGRAFYTTGE11GD1RQAHC CTRPNYNKRKR I H I GPGRAFYT TKN I 1GT I RQAHC TRPNYNKRKR I H I GPGRAFYTTKN I I GT I RQAH TRPNNNTRKS I R I QRGPGRAF VTFGK I GNMRQAH 0.00 1.99 1.14 0.02 0.02 0.03 0.09 0.02 RIHIGPGRAFYTTKNI IGT 0.02 **=** SEQUENCE YNKRKR [H] QRGPGRAF Y T TKN] WN-IIB 0.95 1.60 1.57 0.29 3.36 0.08 0.06 0.05 0.13 0.07 3.11 CTRPNYNKRKR I HIGPGRAF Circular 1.79 2.00 0.88 0.99 0.94 1.11 1.60 2.84 1.82 2.51 inear 2.56 0.82 0.75 0.94 2.07 2.90 2.02 1.46 2.03 2.90 1.75 PND MN/IIIB MN 6-27 + QR HIV-11IIB (34 aa) Linear 2.56 0.98 0.87 2.03 2.20 1.49 1.54 2.96 1.84 JR-CSF (fusion protein) ISOLATE JR-CSF Circular (rgp120) 2.03 2.73 3.00 3.56 . 19. 3.08 2.03 3.11 circular MN 11-30 MN 21-40 1-20 MN linear SF162 (447-52D 8.27.3 4117C 41480 838 1006 694 419 ₹ ₹ 皇 FIG. 6B FIG. 6A 0 ပ 8 GROUP

SYNTHETIC PEPTIDE

FUSION PROTEIN

XENOMOUSER

Mabs

HuMabPs

Docket No. Attorney

Tel: (212)-596-9000

8/11

% INHIBITION OF BINDING BY BIOTINYLATED_

	70 114111	יוום וט ווטוווטו	אט וט טווטו	MINICALED
COMPETING Mab	sCD4	CD4bs 38G3/A9	Conf-B 63G4/E2	gp120-C 97B1/E8
38G3/A9	86	91	-29	ND
35F3/E2	86	90	-22	ND
55D5/F9	87	8 5	-18	ND
28A11/B1	82	ND	ND	ND
46D2/D5	62	ND	ND	ND
67G6/C4	61	ND	ND	ND
38B5/C9	5	-32	84	ND
39H10/A11	0	-32	91	ND
40D3/C11	9	-26	90	ND
49B11/A1	12	-29	90	ND
52G5/B9	19	-37	90	ND
56C4/C8	17	-45	88	ND
57H5/D7	32	-15	90	ND
63G4/E2	27	-24	91	ND
· .	13	-46	81	-35
•	-1	-23	56	-34
65B12/C5	20	-22	40	-31
85G11/D8*	14	-3	0	65
87E4/A8*	20	-11	-3	70
97B1/E8*	20	-13	-1	71
5145A	93	. ND	ND	ND
4117C	30	ND	ND	ND
	38G3/A9 35F3/E2 55D5/F9 28A11/B1 46D2/D5 67G6/C4 38B5/C9 39H10/A11 40D3/C11 49B11/A1 52G5/B9 56C4/C8 57H5/D7 63G4/E2 55E4/H1 57B6/F1 65B12/C5 85G11/D8* 87E4/A8* 97B1/E8*	COMPETING Mab sCD4 38G3/A9 86 35F3/E2 86 55D5/F9 87 28A11/B1 82 46D2/D5 62 67G6/C4 61 38B5/C9 5 39H10/A11 0 40D3/C11 9 49B11/A1 12 52G5/B9 19 56C4/C8 17 57H5/D7 32 63G4/E2 27 55E4/H1 13 57B6/F1 -1 65B12/C5 20 85G11/D8* 14 87E4/A8* 20 97B1/E8* 20	CD4bs 38G3/A9 38G3/A9 86 91 35F3/E2 86 90 55D5/F9 87 85 28A11/B1 82 ND 46D2/D5 62 67G6/C4 61 ND 38B5/C9 539H10/A11 0 -32 40D3/C11 9 -26 49B11/A1 12 -29 52G5/B9 19 -37 56C4/C8 17 -45 57H5/D7 32 -15 63G4/E2 27 -24 55E4/H1 13 -46 57B6/F1 -1 -23 65B12/C5 20 -22 85G11/D8* 14 -3 87E4/A8* 20 -13 5145A 93 ND	COMPETING Mab sCD4 38G3/A9 63G4/E2 38G3/A9 86 91 -29 35F3/E2 86 90 -22 55D5/F9 87 85 -18 28A11/B1 82 ND ND 46D2/D5 62 ND ND 67G6/C4 61 ND ND 38B5/C9 5 -32 84 39H10/A11 0 -32 91 40D3/C11 9 -26 90 49B11/A1 12 -29 90 49B11/A1 12 -29 90 52G5/B9 19 -37 90 56C4/C8 17 -45 88 57H5/D7 32 -15 90 63G4/E2 27 -24 91 55E4/H1 13 -46 81 57B6/F1 -1 -23 56 65B12/C5 20 -22 40 87E4/A8* </th

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		R5	CLADE	В	χ	4 CLADE	В	CLAE	DE E 9/11
EPITOPE	Mab	SF162	BoL	JR-FL	MN	IIIB	SF2	93TH975	CM235
	8.27.3	++	++	++	++	-	++	_	_
V 3	6.7 8E11/A8	++	++	++	+ +	- -	-	- -	- -
]	6.1	++	+	+	+	-	-	-	-
	35D10/D2 40H2/C7	++	-	-	-	-	-	-	-
J	43A3/E4	++	_	-	_	-	-	- -	-
	43C7/B9 45D1/B7	++	-	-	-	-	-	-	-
V1 LINEAR	46E3/E6	++	_	_	-	_	-	- -	-
	58E1/B3 64B9/A6	++	-	-	-	-	-	-	-
	69D2/A1*	++ +	_	-	_	_	-	-	. - -
	82D3/C3*	+	-	-	-	-	-	-	-
V2	8.22.2	++	++	++	-	-	-	-	-
]	28A11/B1	++	+	+	++	++	+	-	-
	35F3/E2 38G3/A9	++	++	+	++	++	+	-	-
Conf A CD4bs	55D5/F9	++ ++	++ ++	+ +	++ ++	++ ++	+	-	-
	46D2/D5	++	+	- [+	++	+	_	-
	67G6/C4*	+	_	-	_	_	_	_	-
	39H10/A11	++	+	+	+	++	+	+	+
	63G4/E2	++	+	+	+	++	+	+	+
	38B5/C9	++	+	+	++	++	- [+	-
	52G5/B9 55E4/H1	++ ++	+ +	+ +	+ +	++	-	+	-
Conf B	49B11/A1	++	+	+	+	++	-	+	-
00111 2	57H5/D7	++	+	+	+	+	-	+	-
	40D3/C11 56C4/C8	++	<u>+</u> - [+ +	+ .	++	_ [+ +	_
	65B12/C5	+	L		+	+	_ L		_
	57B6F1	++]		Į [
]					+	+	-	-	-
	97B1/E8*	+	+	+	+	+	+	-	-
gp120 C	87E4/A8*	+	+	+	+	+	-	-	-
0041	85G11/D8*	+	+		+			-	-
CD4bs	51450	++	++	+	++	++	++	- L	+

FIG.8

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ANTIBODIES WITH NEUTRALIZING ACTIVITY AGAINST PRIMARY HIV-1 STRAINS AND NOVEL HIV-1
NEUTRALIZING ANTIBODIES
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		10/11	
EPITOPE	Mab	CROSS-REACTIVITY	SF162 ND ₅₀
NEUTRALIZ	ING XENOMOUSE R	Mabs	
V1 Linear	35D10/D2 40H2/C7 43A3/E4 43C7/B9 45D1/B7 46E3/E6 58E1/B3 64B9/A6 69D2/A1* 82D3/C3*	SF162	0.27 1.9 3.2 1.4 1.9 0.30 0.55 0.29 4.5 1.2
V2 Linear	8.22.2	SF162 BaL JR-FL	48
V3 Linear	8E11/A8	SF162 Bal JR-FL MN	2.6
V3 Conf.	8.27.3	SF162 Bal JR-FL MN SF2	0.11
Conf. A CD4bs	28A11/B1 35F3/E2 38G3/A9 55D5/F9	SF162 Bal JR-Fl MN IIIB SF2	35 60 31 37
NON-NEU	TRALIZING XENOM		
V3 Linear	6.1 6.7	SF162 Bal JR-FL MN	>50 >50
Conf. A CD4bs	46D2/D5 67G6/C4*	SF162 Bal MN IIIB SF2 SF162	>>200 >>200
	39H10/A11 63G4/E2 38B5/C9	SF162 Bal JR-FL MN IIIB SF2 93TH975 CM235	>>200 >>200 >>200 >>200
Conf. B	52G5/B9 55E4/H1 57H5/D7 40D3/C11 49B11/A1	SF162 Bal JR-FL MN IIIB 93TH975	>>200 >>200 >>200 >>200 >>200 >>200
	56C4/C8	SF162 JR-FL MN IIIB 93TH975	>>200
	57B6/F1	SF162 MN IIIB	>>200
	65B12/C5	SF162 Bal MN IIIB	>>200
gp120 C	85G11/D8* 87E4/A8*	SF162 BaL MN SF162 BaL JR-FL MN IIIB	>>200 >>200
gp120 C	97B1/E8*	SF162 Bal JR-FL MN IIIB SF2	>>200
CONT	ROL HuMabPs		
CD4bs	51450	BROADLY REACTIVE	0.14
V2 Conf.	697D	BROADLY REACTIVE	80
V3 Linear	4117c	BROADLY REACTIVE	0.02

FIG.9

	V1	<u>Central</u>	V2	V2 stem	Far Docket N Attorney	Applicant
8.22.2 Reactive	active				lo.	ts on No.
SF162	HCTNLKNATNTKSSNWKEMDR SEO 10 NO. 10	GEIKNCSF	KVTTSIRNKM <u>QKEYALFYK</u> LDVVPIDNDNTS	YKLINC	ANTIBO	Not yet a
CASEA2B	NCIDLRNATNATSNSNTTNTTSSSGGLMMEQ	GEIKNCSF	NITTSIRDKV <u>OKEYALFYK</u> LDIVPIDNPKNSTN	YRLISC	DIES WITH ALIZING AN RI CON	Pinter et a
JR-FL	NCVKDVNATNTTNDSEGTMER	GEIKNCSF	NITTSIRDEV <u>OKEYALFYK</u> LDVVPIDNNNTS	YRLISC	NEUTRAL	
BaL	SEQ ID NO: 20 NCTDLRNATNGNDTNTTSSSRGMVGG SEQ ID NO: 21	GEMKNCSF	NITTNIRGKV <u>OKEYALFYK</u> LDIAPIDNNSNNR	YRLISC	FOR THE EFFIC IZING ACTIVIT Reg. No.	Confirmation Filed
8.22.2 No	8.22.2 Nonreactive				Y AGAINST	
HXB2d	KCTDLKNDTNTNSSSGRMIMEK	GEIKNCSF	NISTSIRGKVQKEYAFFYKLDIIPIDNDTTS	YKLTSC	ATION OF I	Not yet as
MN-ST	NCTDLRNTTNTNNSTANNNSNSEGTIKG	GEMKNCSF	NITTSIRDKMQKEYALLYKLDIVSINDSTS	YRLISC	NOVEL HU	ntly herewit
SF2	SEG ID NO: 23 NCTDLGKATNTNSSNWKEEIK SEG ID NO: 24	GEIKNCSF	NITTSIRDKIQKENALFRNLDVVPIDNASTTTNYTN	YRLIHC	MAN MONOCLO AINS AND NOVI	h Sheet
		FIG. 10			SMAL	11 of 11